SINGLE CELL HETEROGENEITY
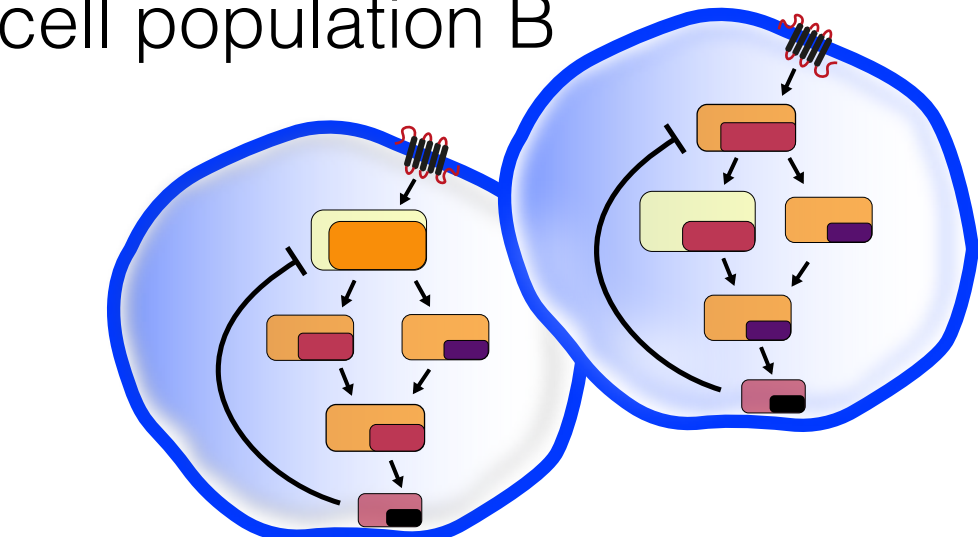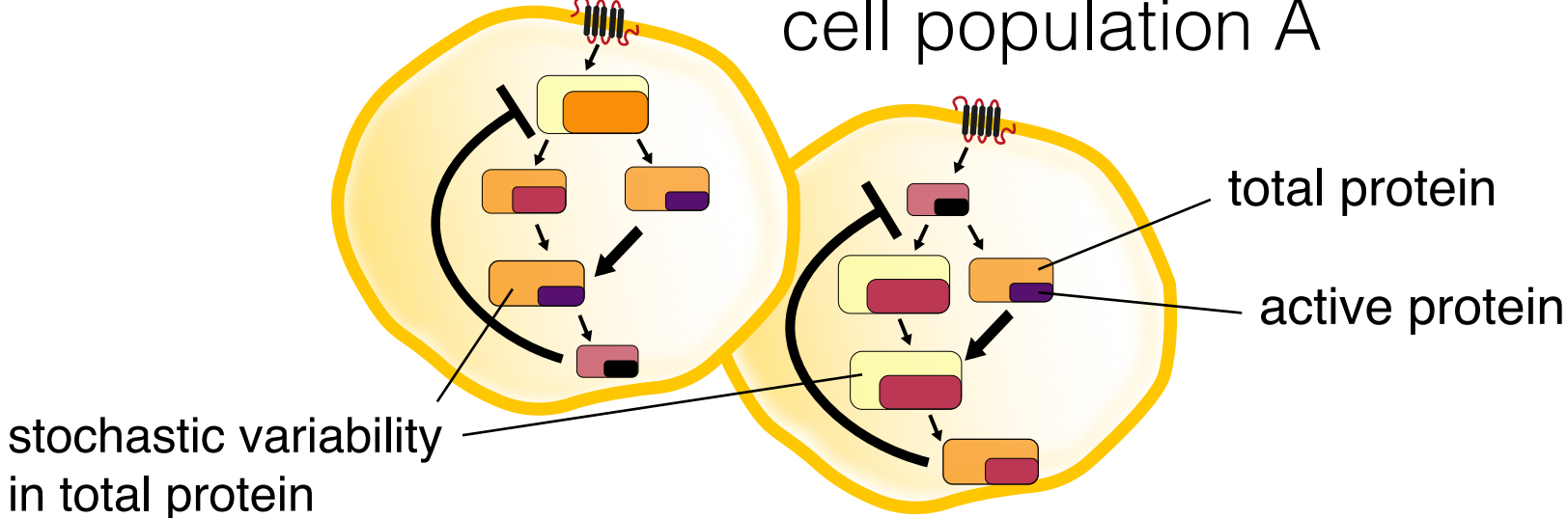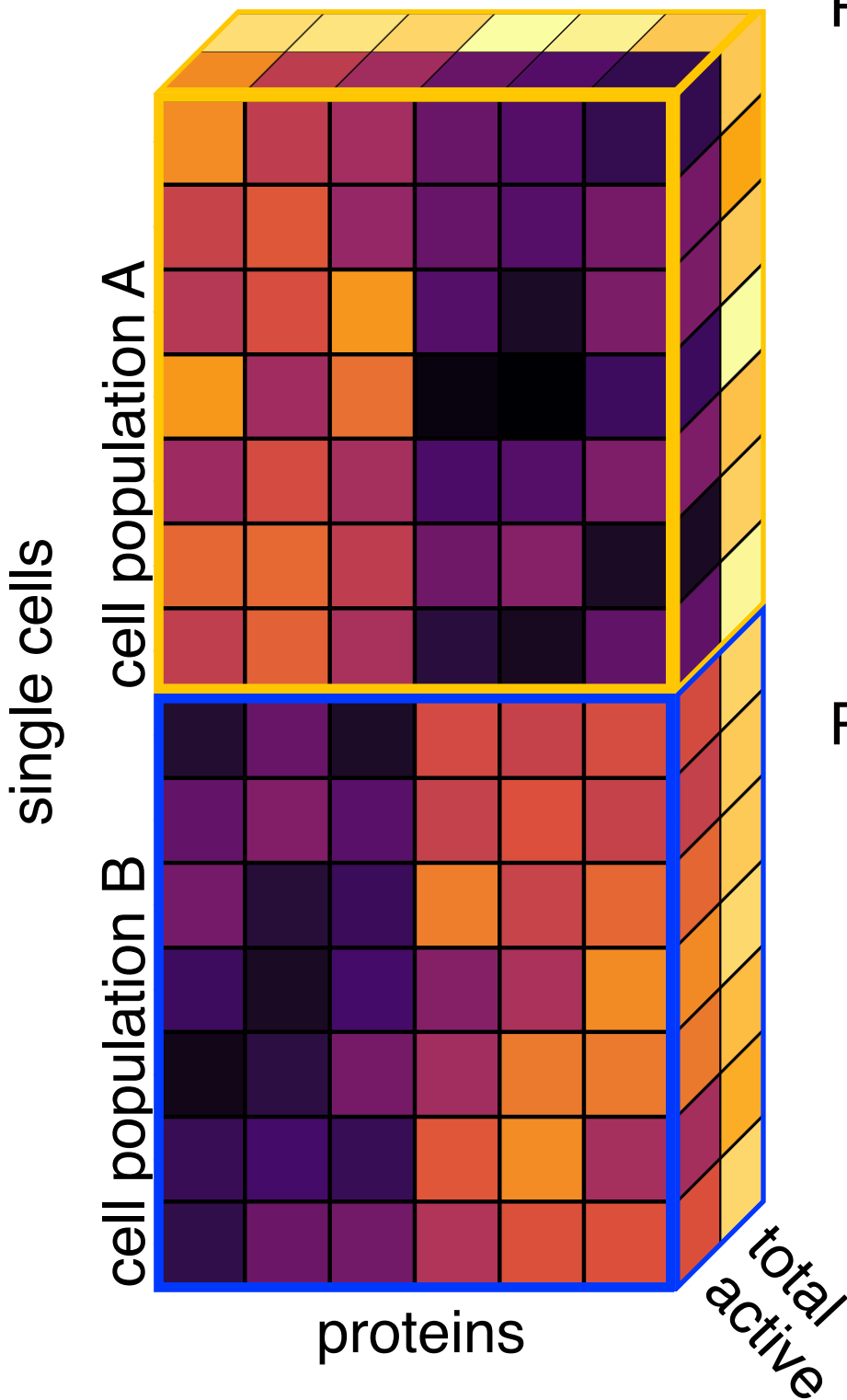
stochastic differences in total protein as 'natural perturbation experiments'

cell population A

total protein

active protein

stochastic variability in total protein

cell population B

INPUT:

CELL - PROTEIN MATRIX

single cells

cell population A

cell population B

proteins

total active

OPTIONAL:

PERTURBATIONS:
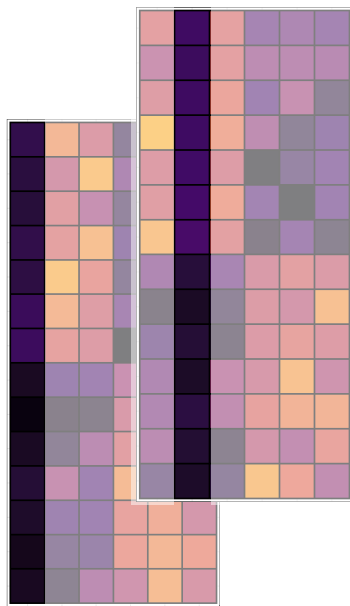
PRIOR NETWORK:
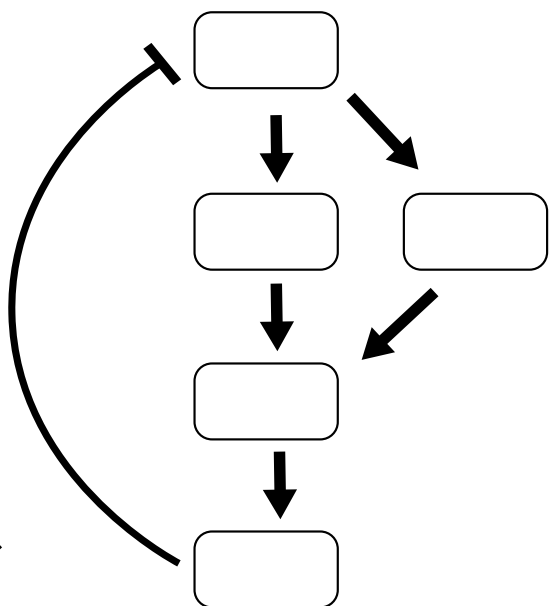
ALGORITHM:

Describe active protein counts in every cell:

R_j

r_{ij}

R_i^{tot} R_i s_i

for a in cells **do**
   for a in cells **do**
      for i in proteins **do**
         $R_{i,a} \approx \sum_{j \neq i} r_{ij} \cdot R_{j,a} + s_i \cdot R_{i,a}^{tot}$
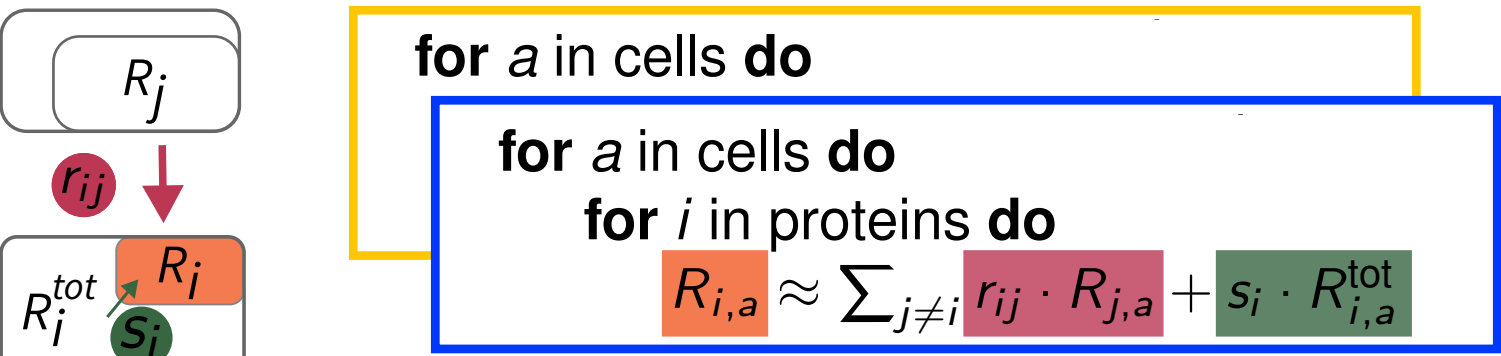
deviation of active protein i from population mean (R_i) =

influence of upstream active protein deviation +

influence of total protein deviation (R_i^{tot})

Minimize objective function:
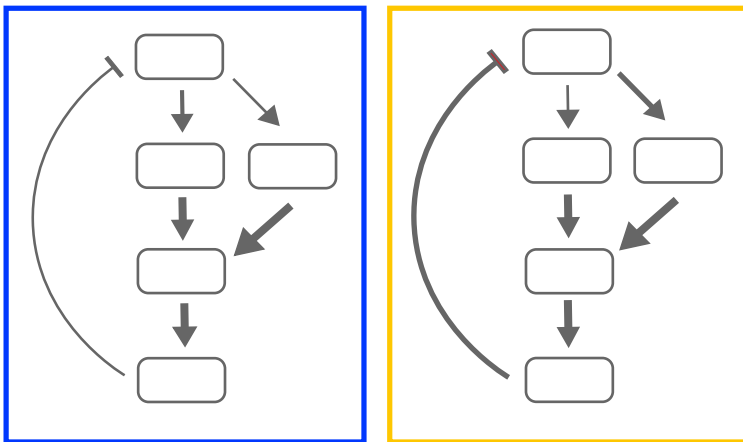
scMRA:
   Fitting error +
   penalty on number of edges +

scCNR:
   Fitting error **A** + Fitting error **B** +
   penalty on number of edges +
   penalty on number of non-equal edges

OUTPUT:

- interaction strength matrix (r)
- sensitivity to total protein (s)

scMRA
individual reconstructions per population

scCNR
one combined reconstruction